Acute Rate Control in Atrial Fibrillation With Left Ventricular Dysfunction
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Clinical Significance of Tachycardia Associated With Atrial Fibrillation (AF)
It is well known that AF is often associated with heart failure (HF) and the involvement of AF not only causes symptoms such as palpitations and chest discomfort, but also worsens existing HF symptoms. Moreover, the rapid ventricular response caused by supraventricular tachycardia, including AF, by itself can induce left ventricular (LV) systolic dysfunction (ie, tachycardia-induced cardiomyopathy). AF with rapid ventricular response also impairs LV filling through loss of active atrial contraction and shortening of diastole.

Rate Control or Rhythm Control in AF With Rapid Ventricular Response
AF with rapid ventricular response is a situation in which physicians are at a loss in their choice of treatment, especially when LV systolic dysfunction is present. With regard to the management of rapid AF, either a rhythm control or rate control strategy must be chosen. The RACE, AFFIRM and J-RHYTHM studies demonstrated that there is no difference between rhythm control and rate control in terms of mortality and morbidity. In patients with chronic HF, the AF-CHF study also revealed that a routine strategy of rhythm control does not reduce the rate of death from cardiovascular causes, as compared with a rate-control strategy. In the acute setting, if the patient’s hemodynamics are unstable, rhythm control by electrical cardioversion may be chosen. Even when hemodynamics are maintained, if tachycardia is sustained, further deterioration may occur, especially in patients who already have LV dysfunction. In such a case, prompt rate control must be attempted to prevent further deterioration of cardiac performance. However, the strategy for rate control for AF in patients with LV systolic dysfunction is not fully established.

Rate Control Therapy (Table)
For rate control of rapid AF, digoxin, nondihydropyridine calcium antagonists, amiodarone or β-blockers can be used. Digoxin is the most popular drug for rate control and seems to be suitable in patients with LV systolic dysfunction because of its positive inotropic effect. However, observational studies indicate that the use of inotropic drugs for acute decompensated HF is associated with poor prognosis. In the DIG study, digoxin did not improve survival in patients with chronic HF. Moreover, a higher plasma concentration of digoxin can increase mortality. Chronic kidney disease, which is very frequently associated with HF, is a relative contraindication for digoxin due to the increased risk of toxicity in these patients. Thus, use of digoxin for rate control in the acute phase of rapid AF may negatively affect the prognosis of patients with accompanying LV systolic dysfunction. Amiodarone effectively converts AF to sinus rhythm, as well as controlling the ventricular response and is recommended by guidelines for acute rate control of AF in patients with LV systolic dysfunction. However, because of its unique pharmacokinetics and possible adverse events, amiodarone is not a drug to be used lightly by the average cardiologist in Japan. Nondihydropyridine calcium antagonists such as diltiazem and verapamil are also used for rate control of rapid AF. These drugs can promptly and safely decrease the ventricular response in AF patients with preserved ejection fraction (EF). However, these agents may worsen HF caused by LV systolic dysfunction through their negative inotropic effect. Moreover, sustained hypotension may occur with overdosing because of their vasodilating action.

Use of β-blockers in the acute phase, on the other hand, may be reasonable in terms of cardioprotection of patients with LV dysfunction. However, the high dose of β-blocker that is required to efficiently lower the ventricular rate may induce further deterioration in LV function and hemodynamics. If a very short-acting β-blocker is used, dose adjustment becomes easier and it can be used safely by step-by-step up-titration in patients with LV dysfunction. Once overdose is suspected, simply discontinuing the drug can rapidly turn things around.

In this issue of the Journal, Nagai et al demonstrate that landiolol, which is already reported to have been safely and effectively used in patients with HF, can also safely lower the ventricular rate in patients with rapid AF and LV systolic dysfunction and that this rate control effect of landiolol is superior to that of digoxin. Recently, Fonarow et al reported initiation of β-blocker during hospitalization improved the prognosis in HF. Because the average length of hospital stay is only 5 days in the USA, which is much shorter than that in Japan, this indicates that earlier is better for the initiation of β-blocker therapy in patients with HF. In patients with moderate to severe HF (ie, >class III), which is an inclusion criteria of the J-Land study, the sympathetic nervous system is more activated than in mild HF and this activation leads to the poor prognosis of these classes of HF. Therefore, from the standpoint of cardioprotection, a
**Target Heart Rate**

In the J-Land study, the endpoint was defined as the percentage of patients with both a heart rate <110 beats/min and >20% decrease from baseline at 2h after drug administration. The rationale for that endpoint was based on the RACE II study. In the RACE II study, the target heart rate was 110 beats/min for the lenient control group, and 80 beats/min for the strict control group. There was no difference in survival between these groups and so lenient control was supported. However, RACE II was designed for patients with permanent AF in a chronic setting and patients with unstable HF, defined as NYHA class IV or HF necessitating hospital admission less than 3 months, were excluded. Moreover, the mean EF of the involved patients was 52% and patients with NYHA class III or more, which was the inclusion criteria in J-Land, comprised only 4–5% of RACE II. Therefore, it is not entirely reasonable to apply a target heart rate <110 beats/min for AF in the acute setting and the target heart rate warrants further discussion.

In conclusion, acute rate control by intravenous landiolol throws new light on the management of tachycardia associated with AF in patients with LV dysfunction. Further clinical studies are needed to investigate whether this strategy can improve cardiac performance and survival.

**References**


